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Complication of radiation therapy among patients with positive S. *aureus* culture from genital tract

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ABSTRACT

Aim: The main goal of this investigation was to evaluate the influence of positive *Staphylococcus aureus* culture from the genital tract on patients receiving radiation therapy, suffering from carcinoma of the uterus. The other aim was to observe radiation therapy complications.
Background: Radiation therapy of patients suffering from cervical cancer can be connected with inflammation of the genitourinary tract.
Materials and methods: In years 2006–2010 vaginal swabs from 452 patients were examined. 39 women with positive *S. aureus* cultures were analysed.
Results: Complications and interruptions during radiation therapy were observed in 7 (18.9%) of 37 patients with positive vaginal *S. aureus* culture. One of them, a 46-year-old woman developed pelvic inflammatory disease. None of the six patients who received palliative radiotherapy showed interruption in this treatment. Isolated *S. aureus* strains were classified into 13 sensitivity patterns, of which 8 were represented by 1 strain, two by 2 strains and three by 13, 8 and 6 strains. One strain was diagnosed as methicillin resistant *S. aureus* (MRSA).
Conclusions: The results of the present study show that *S. aureus* may generally be isolated from the genital tract of female patients with neoplastic disease of uterus but is not often observed as inflammation factor of this tract. Comparison of species' resistance patterns may be used in epidemiological studies in order to discover the source of infections and therefore be of profound significance in the prevention of nosocomial infections.

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1. Background

Radiation therapy of patients suffering from cervical cancer can be connected with inflammation of the genitourinary tract.[1] There are a few papers describing the presence of *Staphylococcus aureus* in the genital tract of women.[2] Most of the world literature shows that *S. aureus* is one of the main pathogens responsible for a number of infections in hospital wards with considerable morbidity and mortality.[3–5]

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The Staphylococcus and Micrococcus are genera belonging to the family Micrococcaceae.

Only one species, *S. aureus*, is an important primary pathogen. The other staphylococci lack primary pathogenicity and are reported to the physician as coagulase negative staphylococci (CNS).

The main site of *S. aureus* in humans is the nasal cavity. Nasal carriers in the general population can be divided into two groups: persistent carriers (20–30% of the population yield *S. aureus* from the nasal cavity at all times) and intermittent carriers (20–30% carry *S. aureus* for a few days or weeks). The remaining part of the population is noncarriers.[6]

The aim of bacteriological examination is to determine whether *S. aureus* was the causative agent of infection and what antimicrobial drugs can be used for treatment.

2. Aim

The main goal of this investigation was to evaluate the influence of positive *S. aureus* culture from the genital tract on patients receiving radiation therapy, suffering from carcinoma of the uterus. The other aim was to observe radiation therapy complications.

3. Materials and methods

Microbiological examinations of the genital tract in patients suffering from colli uteri carcinoma were introduced as a standard method in the Department of Radiotherapy and Gynaecological Oncology at the Greater Poland Cancer Centre. In the years 2006–2010 vaginal swabs from 452 patients were examined. 39 women with positive *S. aureus* cultures were analysed. 37 of them were diagnosed with colli uteri carcinoma of IIB to IVA degree according to the FIGO clinical classification: 6 patients with IIB degree, 1 with IIA, 25 with IIB, 5 with IVA. One of these patients was treated because of metastases from renal carcinoma to vagina and another one because of corpus uteri carcinoma with infiltration to colli uteri. In all cases clinical findings agreed with histopathological diagnosis.

The age of the patients was from 38 to 83 years, 56 years at average.

Among 37 patients with cervical cancer 31 (83.8%) received radical radiotherapy which consisted of external beam radiotherapy combined with intracavitary brachytherapy.

Conformal radiotherapy was administered with 15 MV photons, using a conventional 4-field box technique (opposing anterior and posterior fields, and two opposing lateral fields).

Clinical treatment volume covered tumour of the vaginal fornix and walls, parametria and pelvic lymph nodes. Teletherapy was combined with high-dose brachytherapy (HDR) delivered with anatomy-adjusted applicators (tubes, ovoids, cylinders and needles). The patients were given four fractions of treatment. In the group of radically treated women 25 received concurrent chemotherapy (radiochemotherapy) – cisplatin 40 mg/m^2 given on a weekly basis (5–6 administrations).

Due to advanced stage of cervical neoplastic disease six patients (16.2%) were qualified for a shortened, palliative irradiation of the pelvis with the use of two AP-PA opposing beams technique to be given in one or two series.

Table 1 – Sensitivity of *S. aureus* isolated from vaginal swabs.

The name of drug	The number of strains		
	Sensitive	Intermediately sensitive	Resistant
Penicillin	12	0	27
Oxacillin	38	0	1
Erythromycin	25	9	5
Clindamycin	38	0	1
Gentamicin	38	0	1
Norfloxacin	37	2	0
Levofloxacin	39	0	0
Vancomycin	39	0	0
Teicoplanin	39	0	0
Tetracyclin	33	0	6
Minocyclin	38	0	1
Cotrimoxazole	35	0	4
Fusidic acid	39	0	0
Rifampicin	39	0	0
Nitrofurantoin	39	0	0
Quinupristin/dalfopristin	39	0	0

The vaginal swabs were cultured on the following microbiological media: blood agar, selective media for Gram-negative bacilli, chromagar for yeasts, coccosel agar, cetrimide agar, broth medium. The identification of microorganisms was performed according to standard bacteriological methods, the API 20 identification system (bioMérieux, Marcy l'Etoile, France) was used for confirmation. Antibiotic sensitivity was assessed using the ATB system.

4. Results

Results of 39 isolated *S. aureus* sensitivity tests are presented in Tables 1 and 2. All strains were sensitive to levofloxacin, vancomycin, teicoplanin, fusidic acid, rifampicin, nitrofurantoin and quinupristin/dalfopristin – Table 1. As shown in Table 2, *S. aureus* strains were classified into 13 sensitivity patterns, of which 8 were represented by 1 strain, two – by 2 strains and three by 13, 8 and 6 strains. One strain was diagnosed as methicillin resistant *S. aureus* (MRSA) with sensitivity pattern number 13: 0002222220202222 (Table 2).

Complications and interruptions during radiation therapy were observed in 7 (18.9%) of 37 patients with positive vaginal *S. aureus* culture. Two of them developed urinary tract infection. *Enterococcus faecalis* and *Staphylococcus epidermidis* were isolated from urine cultures of these patients. Pelvic inflammatory disease was observed in one of the 7 patients, a 46-year-old women with third degree inflammation according to the CTC (Common Terminology Criteria for Adverse Events-version 4.0) classification. Clinical symptoms were as follows: temperature from 38 °C to 39.6 °C, abdominal pain, purulent malodorous discharge from the genital tract. Cervical swab culture showed the growth of *S. aureus* with sensitivity pattern number 3: 0212222222222222 (Table 2) and *S. dysgalactiae ssp. equisimilis* sensitive to beta lactam antibiotics, glycopeptides,

Table 2 – Sensitivity patterns of isolated *S. aureus* strains.

Pattern	Antibiotic																No. of strains
	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	
1	0	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	13
2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	8
3	0	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	6
4	0	2	2	2	2	2	2	2	2	0	2	2	2	2	2	2	2
5	2	2	0	2	2	2	2	2	2	2	2	2	2	2	2	2	2
6	0	2	1	2	2	2	2	2	2	0	2	2	2	2	2	2	1
7	2	2	2	2	2	2	2	2	2	2	2	0	2	2	2	2	1
8	2	2	1	2	2	2	2	2	2	2	2	2	2	2	2	2	1
9	0	2	2	2	2	1	2	2	2	2	2	2	2	2	2	2	1
10	0	2	0	2	2	2	2	2	2	2	2	2	2	2	2	2	1
11	0	2	1	2	2	2	2	2	2	0	2	0	2	2	2	2	1
12	0	2	0	0	0	1	2	2	2	0	0	0	2	2	2	2	1
13	0	0	0	2	2	2	2	2	2	0	2	0	2	2	2	2	1

A: penicillin; B: oxacillin; C: erythromycin; D: clindamycin; E: gentamicin; F: norfloxacin; G: levofloxacin; H: vancomycin; I: teicoplanin; J: tetracycline; K: minocycline; L: cotrimoxazole; M: fusidic acid; N: rifampicin; O: nitrofurantoin; P: quinupristin/dalfopristin.
2: Sensitive; 1: intermediately sensitive; 0: resistant.

levofloxacin and clindamycin. The patient was treated according to the sensitivity test of isolated strains.

Three other patients developed vaginitis and collitis – second degree inflammation according to the CTC classification. Vaginal swab culture of two patients showed the growth of *S. aureus* with sensitivity pattern number 1, and number 10 in one patient (Table 2). All of these patients received local treatment. One of the 7 patients who had interruptions during radiation therapy suffered from neutropenia which developed as a complication of complex carcinoma treatment.

None of the six patients who received palliative radiotherapy showed interruption in this treatment.

5. Discussion

Isolated *S. aureus* strains showed high sensitivity to antibiotics. 27 of 39 strains were resistant to 1 or 2 antibiotics from the 16 used for sensitivity tests and 8 strains were sensitive to all of these antibiotics, see Table 2. On the other hand, one strain isolated on 15.03.2008 showed resistance to 6 antibiotics and another one isolated on 18.12.2007 was MRSA. It should be stressed that isolated MRSA was sensitive to vancomycin recommended for treatment of septic patients and to rifampicin and fusidic acid which are used for eradication of MRSA in carriers in some countries, for example in Denmark. The infections caused by MRSA are particularly dangerous because of very high resistance of these bacteria to antibiotics. According to Branger et al., MRSA strains isolated in France were classified into two basic zymotypes while strains isolated in the USA were more diversified.[7] Diversified clones of MRSA were observed in Germany, as well.[8]

The production of beta lactamases is responsible for high proportion of strains resistant to penicillin which were not classified as MRSA. As shown in Table 1, only 12 of 39 strains were sensitive to penicillin. Soon after penicillin became a principal drug in treatment of staphylococcal infections an increase of penicillin resistance was observed, particularly among hospital-associated strains. Zierdt et al. found *S. aureus* strains which produced a particularly high amount of beta lactamases: HBLPSA (hyper beta-lactamase producing *S. aureus*). Oxacillin resistance of HBLPSA is neutralised in the presence of clavulanic acid.[8]

Most penicilinase-releasing strains are sensitive to methicillin, flucloxacillin, ampicillin, vancomycin, teicoplanin, cotrimoxazol, amoxycillin plus clavulanic acid.

Some penicillin-resistant strains are also resistant to methicillin. Methicillin resistant strains *S. aureus* (MRSA) have become the case of the most serious nosocomial infections in a number of hospitals. Carriers of *S. aureus* may develop a nosocomial infection and this species is one of the most frequently observed form of the infection.[9]

The mechanism of resistance to methicillin is related to an alteration in penicillin binding proteins (PBP) produced by resistant strains leading to the development of multidrug resistant *S. aureus*. Chromosomal gene *mec* A is responsible for the presence of a novel PBP in the bacterial membrane.[6] We found one MRSA strain isolated from a patient suffering from cervix cancer. It is worth noting that this strain did not spread in our Department of Radiotherapy and Gynaecologic Oncology. No other patients were infected with MRSA between 2006 and 2010.

In epidemiological studies, aimed at finding the sources of nosocomial infections, it is important to identify the bacterial species involved. One of the methods used to differentiate bacterial species is to determine their sensitivity to drugs. Correct etiological diagnosis and appropriate treatment can have the effect of reducing the numbers of nosocomial infections.

Confirmed radiotherapy of our patients was administered with 15MV photons. According to Tyagi et al., intensity modulated radiotherapy (IMRT) generated by 15 MV photon energies was used for treatment carcinoma of cervix, as well.[10]

6. Conclusion

The results of the present study show that *S. aureus* may generally be isolated from the genital tract of female patients with neoplastic disease of the utreus but is not often observed as inflammation factor of this tract.

Comparison of species' resistance patterns may be used in epidemiological studies in order to discover the source of infections and therefore be of profound significance in the prevention of nosocomial infections.

Conflict of interest

None declared.

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